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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/825,391	04/14/2004	Joan D. Leonard	12780/103	8469

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EXAMINER	
FORD, VANESSA L	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 01/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/825,391	LEONARD ET AL.	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 October 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 November 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

FINAL ACTION

1. Applicant's amendment and response filed October 28, 2005 are acknowledged. Claims 22-23 and 27-28 have been amended. Claims 1-20 have been canceled. Claims 31-36 have been added.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.

Objections Withdrawn

3. In view of Applicant's amendment and response the following objections and rejections have been withdrawn:

a) objection to claims 23 and 28, page 3 , paragraph 3 of previous Office action.

a) objection to claim 22, page 3, paragraph 5 of previous Office action

Rejection Maintained

4. The objection to claims 21-25 is maintained for the reasons set forth on page 3, paragraph 4 of the previous Office Action.

The rejection was on the grounds that Applicant is advised that should claims 21-25 be found allowable, claims 26-30 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Applicant's Argument

Applicant urges that they disagree with the objection. Applicant urges that they defer addressing the objection until allowable subject is indicated.

Examiner's Response to Applicant's Argument

It is the position of the Examiner that claims 21-25 are substantial duplicates of claims 26-30. Thus, the objection will be maintained since Applicant has not addressed the objection.

5. The rejection under 35 U.S.C 103(a) is maintained for claims 21-30 for the reasons set forth on pages 4-7, paragraph 6 of the previous Office Action.

The rejection was on the grounds that Stott et al disclose a quadrivalent vaccine containing the killed antigens of respiratory syncytial virus, parainfluenza virus type 3, *Mycoplasma bovis* and *Mycoplasma dispar* (see the Abstract). Stott et al disclose that the vaccine were emulsified using Freund's incomplete adjuvant and formulated with Tween 80 and merthiolate (page 343).

Stott et al do not teach at least two different *M. bovis* biotypes *Mycoplasma bovis.*

Poumarat et al teach *Mycoplasma bovis* of different biotypes. Poumarat et al teach that Restriction endonuclease analysis (REA) with three enzymes *Sma*I, *Pst*I, and *Bam*I which were used to identify 13 different genomic groups (i.e. biotypes) among 37 *Mycoplasma bovis* strains (see the Abstract). Poumarat et al disclose 37 bovis strains studied gave five different electrophoretic patterns with BamHI, four with *Sam*I and five with *Pst*I (figure 1). Poumarat et al further disclose that based on the combination of the different electrophoretic profiles obtained with the three enzymes, the 37 strains could be classified in 13 genomic groups (table 2).

Stott et al and Poumarat et al as combined above do not teach *Mycoplasma alkalescens.*

Gourlay et al teach that *Mycoplasma alkalescens* is associated with the respiratory tract of bovine (see the Abstract). Gourlay et al teach that *Mycoplasma alkalescens* can colonize the lower respiratory tract but does not produce visible pneumonia (see the Abstract). Therefore, one of ordinary skill in the art could

reasonably conclude that *M. alkalescens* is a secondary agent associated with respiratory infections in bovine.

Stott et al, Poumarat et al, Gourlay et al as combined above do not teach inactivated *Mycoplasma alkalescens.*

However, Chima et al teach that inactivated (formalinized) vaccines have advantages over live vaccines because vaccines comprising live organisms have been shown to result in residual infections three to four months after vaccination (page 120). Additionally, vaccines comprising live organisms have the potential of reversion to full virulence and have been shown to provoke local reaction at the site of inoculation (page 121). Therefore, one of ordinary skill in the art could reasonably conclude that using inactivated components such as inactivated *M. alkalescens* in vaccine compositions is safer than using live organisms.

Therefore, it would be *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to add inactivated *Mycoplasma alkalescens* and inactivated *Mycoplasma bovis* isolates of different biotypes to the vaccine composition as taught by Scott et al because Poumarat et al teach that there is a marked intraspecies genomic heterogeneity among isolates of *Mycoplasma bovis* collected from different geographic origins and that antigenic variability must be taken into account in developing diagnostic and vaccination strategies (page 319) and Stott et al teach that a multicomponent vaccine comprising inactivated components would protect against the important primary pathogens of respiratory disease as well as protecting against secondary agents of respiratory disease (page 342). It would be expected that a vaccine composition comprising inactivated *M. bovis* strains of multiple biotypes, inactivated *Mycoplasma alkalescens*, a pharmaceutically acceptable excipient and a suitable adjuvant would be effect against respiratory infections in cattle because Stott et al teach that major outbreaks of respiratory disease in cattle suggest that other agents are involved in the disease complex. Therefore, it would be advantageous to included additional antigens in vaccines (page 346).

Applicant's Arguments

A) Applicant urges that the cited art teaches away from the claimed invention.

Applicant urges that the claimed invention requires two *Mycoplasma bovis* biotypes.

Applicant urges that Poumarat teaches that antigenic variability is great within *Mycoplasma bovis* groups as across *Mycoplasma bovis* groups and there is no gain in antigenic variability form including more than one type of *Mycoplasma bovis* in a vaccine. Applicant urges that Poumarat teaches away from the claimed invention.

B) Applicant urges that Poumarat's teaching away is especially pertinent in connection with new claims 31-36. Applicant urges that the claims require that the two biotypes of *M. bovis* be genetically different as judged by analysis of DNA or RNA. Applicant urge that Poumarat teaches that genetic differences are irrelevant with respect to antigenicity since Poumarat teaches that there appears to be no relation between genomic variability of *M. bovis* and antigenic variability.

Examiner's Response to Applicant's Arguments

Applicant's arguments filed October 28, 2005 have been fully considered but they are not persuasive.

A) It is the Examiner's position that applicant argues the references individually without clearly addressing the combination of teachings. It is the combination of all of the cited and relied upon references which make up the state of the art with respect to the claimed invention. It must be remembered that Stott et al as well as Poumarat et al teach *Mycoplasma bovis.*

The Examiner disagrees with Applicant's assertion that Poumarat et al teach away from the claimed invention. Poumarat et al teach that variations in expression occurred not only from one strain to another but also within the same lineage of clones from a single cell (see the Abstract). Poumarat et al teach that heterogeneity is great

among the same genomic group and between different genomic groups of *M. bovis* strains (page 318). Poumarat et al suggest that it evident that antigenic variability must be taken into account when developing diagnostic tools as well as vaccination strategies for treating *M. bovis* infections (page 319). Based on the teachings of Poumarat et al, the prior art reference is not teaching away from the claimed invention but actually suggesting why one of ordinary skill in the art would reasonably conclude that multiple strains of *M. bovis* should be present in a vaccine against *Mycoplasma* infections.

B) It is the Examiner's position that Poumarat et al does not teach away from the claimed invention. As stated above, Poumarat et al suggest why one of ordinary skill in the art would reasonably conclude that multiple strains of *M. bovis* should be present in a vaccine against *Mycoplasma* infections. The Examiner's disagrees with Applicant's assertion that "genetic differences are irrelevant with respect to antigenicity". One of ordinary skill in the art would reasonably conclude from reading Poumarat et al that antigenicity among and between *M. bovis* strains is important in developing diagnostic as well as vaccination strategies to treat *M. bovis* infections.

There is nothing on the record to show that the combination of teachings would not suggest the claimed invention.

New Grounds of Rejection Necessitated by Amendment

6. Claims 21-36 are rejected under 35 U.S.C. 103(a) as unpatentable over Stott et al *(The Veterinary Record, October 10, 1987)* in view of Poumarat et al, *(Veterinary Microbiology, Volume 40, 1994, p. 305-321)* in view of Gourlay et al (*Res Vet Sci., September 1979, 27; 233-7)* in view of Chima et al, *(Veterinary Microbiology Vol. 5, pp. 113-122, (1980)* and in further view of Rawadi *(G.A., Characterization of Mycoplasmas by RAPD Fingerprinting, Methods in Molecular Biology, 104:179-187).*

Stott et al disclose a quadrivalent vaccine containing the killed antigens of respiratory syncytial virus, parainfluenza virus type 3, *Mycoplasma bovis* and *Mycoplasma dispar* (see the Abstract). Stott et al disclose that the vaccine were emulsified using Freund's incomplete adjuvant and formulated with Tween 80 and merthiolate (page 343).

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different electrophoretic profiles obtained with the three enzymes, the 37 strains could be classified in 13 genomic groups (table 2).

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Gourlay et al teach that *Mycoplasma alkalescens* is associated with the respiratory tract of bovine (see the Abstract). Gourlay et al teach that *Mycoplasma alkalescens* can colonize the lower respiratory tract but does not produce visible pneumonia (see the Abstract). Therefore, one of ordinary skill in the art could reasonably conclude that *M. alkalescens* is a secondary agent associated with respiratory infections in bovine.

Stott et al, Poumarat et al, Gourlay et al as combined above do not teach inactivated *Mycoplasma alkalescens.*

However, Chima et al teach that inactivated (formalinized) vaccines have advantages over live vaccines because vaccines comprising live organisms have been shown to result in residual infections three to four months after vaccination (page 120). Additionally, vaccines comprising live organisms have the potential of reversion to full virulence and have been shown to provoke local reaction at the site of inoculation (page 121). Therefore, one of ordinary skill in the art could reasonably conclude that using inactivated components such as inactivated *M. alkalescens* in vaccine compositions is safer than using live organisms.

Stott et al, Poumarat et al, Gourlay et al and Chima et al as combined do not teach using DNA polymorphisms to determine different *M. bovis* biotypes.

Rawadi teaches that Mycoplasmas can be characterized by random amplification polymorphic DNA (RAPD) (page 179). Rawadi teaches that RAPD generates a genomic fingerprint that can be used as a "personal signature" of a particular species (page 180).

It would be *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to test for different biotypes of *Mycoplasma bovis* used in a vaccine which is protective in bovine species against *M. bovis* infection as combined above by using DNA polymorphisms because Rawadi teaches that RAPD generates a genomic fingerprint that can be used as a "personal signature" of a particular species (page 180). It would be expected barring evidence to the contrary that RAPD can be used to distinguish between biotypes within a species because Rawadi teaches that difference in DNA fingerprints between two cells can be detected and is a sign of polymorphism during the evolutionary process or mutations that may have occurred throughout the generation (page 180) and Poumarat et al teach that it is evident that antigenic variability must be taken into account in developing diagnostic and vaccination strategies against infections caused by M. bovis (page 319).

Status of Claims

7. No claims allowed.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

9. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 872-9306.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (571) 272-0857. The examiner can normally be reached on Monday – Friday from 9:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (571) 272-0864.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov./>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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January 11, 2006

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